

61-215320

Sep. 25, 1986
INDOMETHACIN OINTMENT

L5: 13 of 22

INVENTOR: SHUNICHI NAITO, et al. (2)

ASSIGNEE: TOYOB0 CO LTD

APPL NO: 60-55015

DATE FILED: Mar. 19, 1985

PATENT ABSTRACTS OF JAPAN

ABS GRP NO: C404

ABS VOL NO: Vol. 11, No. 53

ABS PUB DATE: Feb. 19, 1987

INT-CL: A61K 9*06

ABSTRACT:

PURPOSE: To provide the titled ointment containing indomethacin, white vaseline, a higher alcohol, a W/O-type emulsifier, purified water and a polysorbate or castor oil, effective to suppress the decomposition of indomethacin and storable for a long period.

CONSTITUTION: The objective ointment contains (A) indomethacin .open bracket.chemical name: 1-(p-chlorobenzyl)-5-methoxy-2-methylindole-3-acetic acid.close bracket., (B) white vaseline, (C) a higher alcohol, (D) a W/O-type emulsifier (e.g. sorbitan fatty acid ester), (E) purified water and (F) a polysorbate or castor oil . The decomposition of indomethacin can be suppressed remarkably by the addition of the component F to the ointment base. The polysorbate is especially preferably polysorbate 80 and the amounts of the polysorbate and castor oil in the whole composition are preferably 5. approx. 10wt% and 40. approx. 60wt%, respectively.

=> display history full 11-

(FILE 'USPAT' ENTERED AT 16:26:39 ON 18 JAN 95)
DELETE HISTORY Y

FILE 'JPOABS' ENTERED AT 16:44:12 ON 18 JAN 95

L1	69 SEA (POLYSORBATE OR TWEEN) (W) 80 OR POLYOXYETHYLENE (W) S
ORB	ITAN (W) MONOOLEATE
L2	792 SEA CASTOR
L3	6 SEA L1 AND L2
L4	85922 SEA GLYCERIDE? OR OIL
L5	22 SEA L1 AND L4

Checked L3, L5
JL
1-18-95

=> d 309

309. 3,696,189, Oct. 3, 1972, STABILIZED ANTIBIOTIC AND METHOD; Frank M. Snyder, 424/438, 442, 498; 514/10, 152 [IMAGE AVAILABLE]

=> d 309 bsum(14)

US PAT NO: 3,696,189 [IMAGE AVAILABLE]

L3: 309 of 317

SUMMARY:

BSUM(14)

A wide variety of emulsifiers may be used for this purpose. In general, the emulsifier contemplated for use in accordance with the concepts of the present invention are pharmaceutically acceptable emulsifying agents which have no deleterious effects upon animals, and particularly ruminant animals. Particularly preferred is polysorbate 80 which is a mixture of esters of oleic acid with sorbitol and their mono- and dianhydrides having an acid value below 7.5 and which has been condensed with approximately 20 moles of ethylene oxide per mole of sorbitol. Such emulsifiers are commercially available under the tradename Tween

80. However, a wide variety of other emulsifiers may be used, such as Atmus 300 from Atlas Chemical Company as well as a wide variety of other emulsifying agents formed by the condensation of polyoxyethylene with esters of fatty acids. In general, the amount of emulsifier used is preferably within the range of 2-20 percent of the antibiotic-containing slurry.

=> d 316

316. 3,627,791, Dec. 14, 1971, BIS(AMINOALKYLSULFAMOYL) ANTHRAQUINONES; Johann Grisar, et al., 552/222; 514/934; 552/234 [IMAGE AVAILABLE]

=> d 316 detd(6)

US PAT NO: 3,627,791 [IMAGE AVAILABLE]

L3: 316 of 317

DETDESC:

DETD(6)

A preferred mode of administration for the compounds (active ingredients) of this invention is parenterally such as by normally liquid injectable compositions, e.g., for intramuscular or subcutaneous administration. In such compositions the quantity of active ingredient can vary from about 0.05 to 20 percent by weight of the composition and preferably from about 0.1 to 10 percent by weight. In order to minimize or eliminate irritation at the site of injection, the parenteral compositions can contain a nonionic surfactant such as those having an HLB (hydrophile-lipophile) balance of about 12 to 17. Such formulations can be solutions, suspensions or emulsions in conventional liquid pharmaceutical carriers, e.g., sterile liquids such as water, saline, and aqueous dextrose (glucose) and related sugar solutions. The quantity of surfactant in the formulation can vary from about 5 to 15 percent by weight of the formulation. The quantity of a compound of this invention, either in the base form or a pharmaceutically acceptable acid addition salt in such formulations, can vary over a broad range such as that mentioned hereinbefore, i.e., 0.05 to 20 percent by weight of the formulation. Preferably, the active ingredient is in the base form. The remaining component or components of such formulations can be a normally liquid pharmaceutical carrier, e.g., isotonic aqueous saline, either alone or together with conventional excipients for injectable compositions. The surfactant can be a single surfactant having the above

Best Available Copy

d 309

1. 3,696,189, Oct. 3, 1972, STABILIZED ANTIBIOTIC AND METHOD; Frank M. Wider, 424/430, 442, 498; 514/10, 152 [IMAGE AVAILABLE]

d 309 bsum(14)

PAT NO: 3,696,189 [IMAGE AVAILABLE]

LB: 309 of 317

4MARY:

JM(14)

wide variety of emulsifiers may be used for this purpose. In general, an emulsifier contemplated for use in accordance with the concepts of the present invention are pharmaceutically acceptable emulsifying agents which have no deleterious effects upon animals, and particularly ruminant animals. Particularly preferred is polysorbate 80 which is a mixture of esters of oleic acid with sorbitol and their mono- and anhydrides having an acid value below 7.5 and which has been condensed with approximately 20 moles of ethylene oxide per mole of sorbitol. Such emulsifiers are commercially available under the trademark Tween 80. However, a wide variety of other emulsifiers may be used, such as mus 300 from Atlas Chemical Company as well as a wide variety of other emulsifying agents formed by the condensation of polyoxyethylene with esters of fatty acids. In general, the amount of emulsifier used is preferably within the range of 2-20 percent of the antibiotic-containing carrier.

d 316

5. 3,627,791, Dec. 14, 1971, BIS(AMINOALKYLSULFAMOYL) ANTHRAQUINONES; Hann Grisar, et al., 552/222; 514/934; 552/234 [IMAGE AVAILABLE]

d 316 detd(6)

PAT NO: 3,627,791 [IMAGE AVAILABLE]

LB: 316 of 317

TDESC:

TD(6)

preferred mode of administration for the compounds (active ingredients) of this invention is parenterally such as by normally liquid injectable compositions, e.g., for intramuscular or subcutaneous administration. In such compositions the quantity of active ingredient can vary from about 0.05 to 20 percent by weight of the composition and preferably from about 0.1 to 10 percent by weight. In order to minimize irritation at the site of injection, the parenteral compositions can contain a nonionic surfactant such as those having an HLB (hydrophile-lipophile balance) of about 12 to 17. Such formulations can be solutions, suspensions or emulsions in conventional liquid pharmaceutical carriers, e.g., sterile liquids such as water, saline, and aqueous dextrose (glucose) and related sugar solutions. The quantity of surfactant in the formulation can vary from about 5 to 15 percent by weight of the formulation. The quantity of a compound of this invention, either in the base form or a pharmaceutically acceptable acid addition salt in such formulations, can vary over a broad range such as that mentioned hereinbefore, i.e., 0.05 to 20 percent by weight of the formulation. Preferably, the active ingredient is in the base form. The remaining component or components of such formulations can be a normally liquid pharmaceutical carrier, e.g., isotonic aqueous saline, either alone or together with conventional excipients for injectable compositions. The surfactant can be a single surfactant having the above indicated HLB or a mixture of two or more surfactants wherein such mixture has the indicated HLB. The following surfactants are illustrative of those which can be used in such formulations: (A) Polyoxyethylene derivatives of sorbiten fatty acid esters, such as the Tween series of reactants, e.g., Tween 80, and the like. The Tweens are manufactured by Atlas Powder Company. (B) High molecular weight adducts of ethylene oxide with a hydrophobic base formed by the condensation of ethylene oxide with propylene glycol, e.g., Pluronic F-68 which is manufactured by ICI and Ferrad surfactant is